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Significance of NTM infections in Croatia

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ABSTRACT

Nontuberculous mycobacteria (NTM) are environmental, opportunistic pathogens found in soil and water. NTM are adapted for residence in drinking water distribution systems as they are disinfectant-resistant, surface adherent, and able to grow on low concentrations of organic matter. Reports of NTM infections have been increasing over the past two decades. Of the >150 NTM species reported in the literature, some 25 species have been strongly associated with a variety of human diseases, of which the pulmonary NTM disease (PNTM) is the most frequent. The distribution of NTM species differs strongly by region and it is generally accepted that NTM species differ in their clinical relevance. Further, NTM differ strongly in their growth rate, temperature tolerance, and drug susceptibility, making the correct species identification a very important step in the process of diagnosis. Because NTM are environmental bacteria, the diagnosis of PNTM is complex and requires good communication between clinicians, radiologists, and microbiologists. Extensive microbial resistance, often misleading in vitro drug susceptibility patterns, and complicated treatment regimens are just some of the factors adding to the frustration of the clinical management of NTM diseases. To prevent unwarranted diagnoses and treatment of NTM disease as well as unnecessary diagnostic delay, it could be helpful to use separate, more stringent criteria for species of low relevance, and less stringent criteria for species considered to be of high clinical relevance in the local setting, namely: isolation of *Mycobacterium kansasii* (worldwide) and *Mycobacterium malmoense* (north-western Europe) from pulmonary specimens usually indicates disease, whereas *Mycobacterium goodii* and *Mycobacterium simiae* typically represent contamination. This approach requires complete and up-to-date insight in locally prevalent NTM and their clinical relevance. In Croatia, all strains of NTM isolated in any laboratory are sent to the National Reference Laboratory for identification. NTM strains have been systematically recorded and reported since 1982. In the last decade, two retrospective analyses were done to assess the clinical relevance of different NTM species and the burden of pulmonary NTM disease. Over the past decade, a 30-fold increase in overall NTM isolation rates and a 4-fold increase in PNTM incidence were observed. *Mycobacterium xenopi* was the most frequently seen causative agent of pulmonary NTM disease, but the degree of clinical relevance (i.e., percentage of patients meeting the diagnosis criteria, per species) was higher for isolates of MAC (66.5%) and *M. kansasii* (57.2%). Only about 30% of the *M. xenopi* isolates represented true disease. Further, interesting regional differences were observed. Clinically relevant NTM isolates were significantly more often found in the coastal region of Croatia, and the average annual incidence of the PNTM was twice as high in coastal compared with the continental region. The overall burden of PNTM in

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Croatia is still low compared with tuberculosis. This can, in part, explain the observed lack of knowledge of NTM infections among respiratory specialists. Since these pathogens are increasingly common worldwide, especially in countries where the incidence of tuberculosis is declining, a constant rising of awareness and knowledge is necessary.

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